

diethylenetriaminepentaacetic acid (DTPA) chelates which used carbostyryl as sensitizer. Bailey, et al., Analyst, **109**, (1984) 1449; Ando, et al. Biochim. Biophys. Acta, **1102**, (1992) 186; and Heyduk et al., Anal. Biochemistry, **248**, (1997) 216 also describe DTPA lanthanide chelates which contain different sensitizers. Additional DTPA chelates with other sensitizers and other tracer metals are known for diagnostic or imaging use (e.g., EP 0450742 A1).

On page 11, please replace Example 1 (lines 10 - 25) with the following paragraph:

Example 1

Preparation of 3AAP-DTPA (1) and 3AAP-DTPA-4APEA (5)

To a solution of DTPA (143 mg, 0.4 mmol) in 10 mL dry DMSO and 2 mL dry triethylamine was added a solution of 3-aminoacetophenone (3AAP, 54 mg, 0.4 mmol) in 5 mL DMSO. The mixture was stirred at room temperature for 0.5 h and then treated with a solution of 4-aminophenethylamine (4APEA, 53 mg, 0.4 mmol) in 5 mL DMSO. The mixture was allowed to stir at room temperature for an additional 3 h and then evaporated to dryness. The oily residue was chromatographed on reversed-phase C18 hplc (using a step gradient of 0 to 60% acetonitrile in 0.1% TFA buffer) to give, after lyophilization, **1** as a cream colored solid and **5** as a pale yellow solid. Compound **1** was obtained in 59 mg yield. ¹H-NMR (CD₃OD) : δ 2.60 (3H, s), 3.1-3.5 (10H, m), 3.6 (2H, s), 3.65 (2H, s), 3.71 (2H, s), 4.42 (2H, s), 7.42 (1H, dd), 7.75 (1H, dd), 7.83 (1H, dd), 8.31 (1H, d); MS: m/z 511 (M-H). Compound **5** was obtained in 16 mg yield. ¹H-NMR (CD₃OD): δ 2.62 (3H, s), 2.73 (2H, t), 3.21 (2H, t), 3.3-3.55 (12H, m), 3.65 (2H, s), 3.74 (2H, s), 4.35 (2H, s), 7.13 (4H, s), 7.41 (1H, dd), 7.75 (1H, dd), 7.83 (1H, dd), 8.32 (1H, d); MS: m/z 682 (M+ 3NH₄), 683 (MH+ 3NH₄).

On page 11 bridging page 12, please replace Example 2 (page 11, line 27 to page 12, line 4) with the following paragraph:

Example 2

Preparation of 4AAP-DTPA-APEA-ITC (6).

To a solution of 4AAP-DTPA-APEA (**3**, 12 mg, 0.019 mmol) in 10 mL of 0.5 N HCl was added 4mL of thiophosgene (85% in CCl₄). The two phase reaction was allowed to stirred vigorously for 1 h. The mixture was worked up by separating the layers in a separatory funnel and the aqueous solution was washed by additional

methylen chloride and then chromatographed on a small reversed-phase C18 column to give the thioisocyanate product (**6**), an off-white solid in 10 mg yield after lyophilization. ¹H-NMR (CD₃OD): 2.60 (3H, s), 2.72 (2H, t), 3.20 (2H, t), 3.3-3.5 (12H, m), 3.65 (2H, s), 3.74 (2H, s), 4.34 (2H, s), 7.12 (4H, s), 7.41 (1H, ss), 7.74 (1H, dd), 7.84 (1H, dd), 8.20 (1H, d); MS: m/z 724 (M+3NH₄), 725 (MH+ 3NH₄); IR: 2108 cm⁻¹ (S=C=N stretch).

On page 12, please replace Example 3 (lines 6 - 20) with the following paragraph:

Example 3

Preparation of 4ABP-DTPA (4**) and 4ABP-DTPA-4APEA (**12**)**

To a solution of DTPA (179 mg, 0.5 mmol) in 5 mL of dry DMSO and 3 mL of dry triethylamine was added a solution of 4-aminobenzophenone (4ABP, 99 mg, 0.5 mmol) in 5 mL DMSO. The mixture was stirred for 0.5 h and treated with a solution of 4-aminophenethylamine (4APEA, 68 mg, 0.05 mmol) in 5 mL DMSO. After an additional 3 h stirring at room temperature, the mixture was evaporated to dryness. The oily residue was chromatographed on reversed-phase C18 hplc (using a step gradient of 0-60% acetonitrile in 0.1% TFA buffer) to give **4** as a cream colored solid and **12** as a pale yellow solid. Compound **4** was obtained in 57 mg yield. ¹H-NMR (CD₃OD): δ 3.2-3.5 (10H, m), 3.60 (2H, s), 3.63 (2H, s), 3.74 (2H, s), 4.43 (2H, s), 7.53 (2H, m), 7.62 (1H, dd), 7.76 (2H, m), 7.8 (4H, s); MS: m/z 573 (M+H). Compound **12** was obtained in 47 mg yield. ¹H-NMR (CD₃OD): δ 2.73 (2H, t), 3.25 (2H, t), 3.3-3.5 (12H, m), 3.67 (2H, s), 3.73 (2H, s), 4.3 (2H, s), 7.23 (4H, s), 7.55 (2H, m), 7.64 (1H, dd), 7.8 (2H, m), 7.83 (4H, m); MS: m/z 691 (M+H).

REMARKS

By way of background, Applicants filed an Amendment and Reply Under 37 CFR 1.111 on July 2, 2002 (hereinafter "July 2002 Response"), in response to an Office Action mailed on January 2, 2002 in the present application. The July 2002 Response included certain amendments to the specification and claims, and accompanying remarks addressing matters raised by the Examiner in the January 2, 2002 Office Action.